

08/095,801, filed July 20, 1993, now abandoned, which is continuation of application Serial No. 07/501,904, filed March 29, 1990, now abandoned, which is a continuation-in-part of application Serial No. 07/355,027, filed May 19, 1989, now abandoned, which are all hereby incorporated by reference.--

#### REMARKS

Claims 40, 41, 43, 44 and 46-49 are pending.

In the October 10, 1997, Office Action, the Examiner rejected claims 40, 41, 43, 44 and 46-49 under 35 U.S.C. §102(e) as allegedly being anticipated by Stetler-Stevenson (U.S. Patent No. 5,595,885). Specifically, the Examiner alleged that Figure 8 of the Stetler-Stevenson disclosed amino acids 1-194 in Figure 2 of the present application. See page 2, paragraph 7, of the Office Action. The Examiner also alleged that Stetler-Stevenson taught the cloning of a cDNA encoding TIMP-2 and that a cDNA clone encoding the amino acid sequence of TIMP-2 may be expressed in any suitable expression system, either prokaryotic or eukaryotic. Id.

In response, Applicants respectfully traverse the rejection. Applicants assert that the rejection should be withdrawn because the Examiner improperly relies on Stetler-Stevenson as the basis for a rejection under §102(e). To properly reject claims under 35 U.S.C. §102(e), the Examiner must find that the claimed invention was described in a patent which was granted on an application by another filed in the United States before the application under examination. Applicants assert that the disclosure relied upon for the present rejection was first presented in an application that was filed in the United States after the present application.

Applicants first disclosed the claimed invention in a priority application, U.S. Serial No. 07/355,027 (the '027 application), which was filed on May 19, 1989. The '027 application disclosed not only amino acids 1-194 in Figure 2 of the present application, but also a cDNA clone encoding TIMP-2 protein and how to express the protein. Therefore, the application that was filed May 19, 1989, disclosed the claimed invention.

Stetler-Stevenson claims the benefit of U.S. Serial No. 08/039,525, filed March 29, 1993, which is a continuation application of U.S. Serial No. 07/395,453, filed August 18, 1989, which is a continuation-in-part of U.S. Serial No. 07/380,431, filed July 17, 1989 (the '431 application), which is a continuation-in-part of U.S. Serial No. 07/326,334, filed March 21, 1989 (the '334 application).

The Examiner apparently accorded Stetler-Stevenson a §102(e) date of March 21, 1989, based on the '334 application's filing date. Although that March 21, 1989, filing date is before the May 19, 1989, filing date of the present application, Applicants assert that the Examiner improperly accorded Stetler-Stevenson a §102(e) date of March 21, 1989. The '334 application fails to describe the claimed invention, since it does not disclose the cDNA sequence, the cloning of a cDNA encoding TIMP-2, and expression of this protein. Moreover, the '334 patent fails to show an amino acid sequence corresponding exactly to Figure 8 of Stetler-Stevenson. In fact, the amino acid sequence shown in Figure 2 of the '334 application (bottom row of the attached Exhibit 1) differs significantly from Figure 8 in Stetler-Stevenson and from amino acids 1-194 in Figure 2 according to the presently claimed invention. After comparing the amino acid sequences of Figure 2 of the '334 application to Figure 2 of the presently

claimed invention, one sees that amino acids at positions 34, 39, 69, 75, 79, 96, 124, 149, 151, 153, 171-174 and 176-180 of Figure 2 of the presently claimed invention differ from the amino acids at the corresponding positions in Figure 2 of the '334 application. See the attached Exhibit 2: comparison of the amino acid sequences.

Further, the amino acid sequence in Figure 2 of the '334 application does not disclose amino acids 41-57, 82-94 and 154-162 in Figure 2 of the presently claimed invention.

Id. Also, the amino acid sequence in the '334 application contains a discrepancy at positions 181 to 185 of the presently claimed invention in Exhibit 2: eight amino acids are disclosed in the amino acid sequence disclosed in the '334 application that all differ from the four amino acids disclosed at corresponding positions in Figure 2 of the presently claimed invention. Therefore, the '334 application does not disclose amino acids 1-194 of the claimed invention.

Applicants also point out that, although Stetler-Stevenson discusses cloning of a cDNA that encodes TIMP-2 from a melanoma cell and expression of TIMP-2 in host cells, the '334 application does not. Specifically, the '334 application discloses purification of TIMP-2 from melanoma cells and generally states "[t]he complete TCCI protein or TCCI peptides can be produced...by recombinant DNA technology." See page 9, lines 16-18 of the '334 application. However, the '334 application does not describe how to express the protein in such a way to enable one skilled in the art to actually do it.

In view of the deficiencies in the '334 application: the failure to disclose an amino acid sequence according to the present claims, the failure to disclose the cDNA sequence encoding TIMP-2, and the failure to describe how to obtain a cDNA clone

that encodes TIMP-2 or how to express the protein using a cDNA clone, applicants assert that the Examiner may not properly accord Stetler-Stevenson a §102(e) date of March 21, 1989, as the basis for maintaining the §102(e) rejection. The next filing date claimed by Stetler-Stevenson is July 17, 1989. Since July 17, 1989, is after the May 19, 1989, filing date of the subject application, the Examiner cannot maintain the §102(e) rejection. Accordingly, Applicants respectfully request reconsideration and withdrawal of the Examiner's rejection.

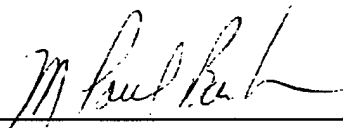
Applicants note that the §102 (e) rejection was the sole basis for rejecting the present application. Applicants maintain that the subject application is in condition for allowance and request that the Examiner issue a timely allowance of pending claims 40, 41, 43, 44 and 46-39.

If any further extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this response, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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By: \_\_\_\_\_

  
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Upper row: Previously known sequence of human tissue inhibitor of metalloproteinase (TIMP)

Lower row: Novel sequence of invention indicating scattered short homologies to TIMP and conservation of cysteines.

07/026334

5	10	15	20	25	30
C	T	C	V	P	P
C	S	C	S	P	V
H	P	Q	Q	A	F
C	N	S	D	L	V
I	R	A	K	F	V
G	T	P	E	V	N
K	E	V	D		
35	40	45	50	55	60
Q	T	T	L	Y	Q
R	Y	E	I	K	M
T	K	M	Y	K	G
F	Q	A	L	G	D
A	A	D	I	R	F
S	G	N	P	I	Y
G	N	N	I		
K	D	I	E	F	
65	70	75	80	85	90
V	Y	T	P	A	M
E	S	V	C	G	Y
F	H	R	S	H	N
R	S	E	E	F	L
I	A	G	K	L	Q
I	Y	T	A	P	S
E	A	V	C	G	V
E	L	D	V	E	G
K					
95	100	105	110	115	120
D	G	L	L	H	I
T	T	C	S	F	V
A	P	W	N	S	L
S	L	A	Q	R	R
G	F	T	K	T	Y
K	R	H	I	T	L
C	D	F	I	V	P
W	D	T	L	S	T
T	Q	K	K	S	L
N	H	R	Y		
125	130	135	140	145	150
T	V	G	C	E	E
C	T	V	F	P	C
L	S	I	P	C	K
L	Q	S	G	T	H
C	L	W	T	D	Q
Q	Q	G	C	E	E
C	K	I	T	R	C
P	M	I	P	C	Y
I	S	S	P	D	E
C	L	W	T	D	T
155	160	165	170	175	180
L	L	Q	G	S	E
K	G	F	Q	S	R
H	L	A	C	L	P
R	E	P	G	L	C
T	W	Q	S	L	R
V	V				
K	F	F	A	C	I
K	R	H	I	T	L
C	D	F	I	V	P
W					
185					
S	Q	I	A		
D	X	L	S	S	X
Q	K	Q	E	F	L
D	T	E	D		

EXHIBIT 1

FIGURE 2

Comparison of Amino Acids 1-194 in Figure 2 of the present application (top row) with Amino Acids 1-196 in Figure 2 of U.S.  
Serial No. 07/326,334, filed March 21, 1989 (bottom row)

CSCSPVHPQQ	AFCNADVIR	AKAVSEKVD	SGNDIYGNPI	KRIQYEIDQI	KMFKGPEKDI	EFIYTAPSSA	VCGVSLDVGG
CSCSPVHPQQ	AFCNADVIR	AKAVSEKVD	SGNPIYGNNI	-----	-----KDI	EFIYTAPSEA	VCGVELDVGG
KKEYLIAGKA	EGDGKMHITL	CDFIVPWDTL	STTQKKSLNH	RYQMGCECKI	TRCPMIPCYI	SSPDECLWMD	WVTEKNINGH
K-----	-----KRHITL	CDFIVPWDTL	STTQKKSLNH	RYQMGCECKI	TRCPMIPCYI	SSPDECLWTD	TVV-----
QAKFFACIKR	SDGSCAWYRG	AAPPKQEFLD	IEDP	E			
--KFFACIKR	HITLCDFIVP	KQEFLD	IED				
	WDXLSSXQ						

EXHIBIT 2